

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

LISTING OF CLAIMS:

1-3. (cancelled)

4. (currently amended) A method for ~~in vitro inserting in~~
~~vitro insertion of~~ a nucleic acid of interest initially included in a DNA vector, within a predetermined target nucleotide sequence present in a chromosome contained in a prokaryotic or eukaryotic cell, ~~characterized in that its~~ said method comprises the following steps of:

- a) contacting the DNA vector comprising the nucleic acid of interest, and replicating said DNA vector in said prokaryotic or eukaryotic cell, with a mutagenic agent blocking the DNA replication in the cell;
- b) transfecting said prokaryotic or eukaryotic ~~cells~~ cells with the DNA vector ~~such as obtained at the end of step a); and~~
- c) selecting ~~the~~ prokaryotic or eukaryotic cells for which the nucleic acid of interest has been integrated into the predetermined target nucleotide sequence.

5. (currently amended) AThe method according to claim 4,
~~characterized in that it further comprises the~~further comprising
~~following step of:~~

d) selecting, amongst from the prokaryotic or eukaryotic cells ~~as selected obtained~~ in step c), the cells wherein the DNA vector sequences, other than those of the nucleic acid of interest, were removed.

6. (currently amended) AThe method according to claim 4,
~~characterized in that~~ wherein the mutagenic agent is selected amongst from the group consisting of: N-acetoxy-2-acetylaminofluorene (N-AcO-AAF), an alkylating agent, benzo(a)pyrene-diol-epoxyde (BPDE) ~~as well as~~ and UV irradiation.

7. (currently amended) AThe method according to claim 5,
~~characterized in that~~ wherein the mutagenic agent is N-acetoxy-2-acetylaminofluorene (N-AcO-AAF).

8. (currently amended) AThe method according to claim 7,
~~characterized in that~~ wherein in step a), the N-AcO-AAF is contacted with the DNA vector comprising the nucleic acid of interest, at a concentration adapted for binding at least 10 N-AcO-AAF molecules per molecule of the polynucleotide.

9. (currently amended) A-The method according to claim 8,
~~characterized in that wherein~~ the concentration ~~in~~ of N-AcO-AAF
is adapted for binding at least 50 N-AcO-AAF molecules per
molecule of the polynucleotide.

10. (currently amended) A-The method according to claim 4,
~~characterized in that wherein~~ the nucleic acid of interest to be
inserted into the ~~genome~~ chromosome of the prokaryotic or
eukaryotic cell, being initially included in said DNA vector
comprises respectively at its ~~end~~ 5' terminus and at its ~~end~~ 3'
terminus, sequences ~~with a high identity degree having at least~~
99.5% identity with the corresponding sequences located at the
~~ends~~ 5' terminus and 3' terminus of the target DNA contained in
the chromosome.

11. (currently amended) A-The method according to claim 10,
~~characterized in that wherein~~ the sequences respectively located
at ~~end~~ the 5' terminus and at ~~end~~ 3' terminus of the nucleic acid
of interest are identical respectively to the ~~ends~~ 5' terminus
and 3' terminus of the target DNA contained in the chromosome.

12. (currently amended) A-The method according to claim 4,
~~characterized in that wherein~~ the nucleic acid of interest
included in said DNA vector comprises a selection marker
nucleotide sequence.

13. (currently amended) A The method according to claim 4,
~~characterized in that~~ wherein the nucleic acid of interest
comprises an open reading frame ~~eeding~~ that encodes a protein of
therapeutic interest.

14. (currently amended) A The method according to claim 4,
~~characterized in that~~ wherein the nucleic acid of interest
comprises an open reading frame disrupted by a heterologous
nucleotide sequence.

15. (currently amended) A The method according to claim 4,
~~characterized in that~~ wherein the nucleic acid of interest ~~ees~~
encodes an antisense RNA.

16. (currently amended) A The method according to claim 13,
~~characterized in that~~ wherein the nucleic acid of interest further
comprises a nucleotide sequence with a promoter function, being
functional in the selected prokaryotic or eukaryotic host cell,
under the control of which the open reading frame or the sequence
~~eeding~~ encoding the RNA included in said nucleic acid of interest
is operably arranged.

17. (currently amended) A The method according to claim 4,
~~characterized in that~~ wherein the polynucleotide-nucleic acid

comprising the nucleic acid of interest comprises a marker nucleotide sequence located, in said polynucleotide, outside the nucleotide sequence of the nucleic acid of interest.

18. (currently amended) A-The method according to claim 4,
~~characterized in that~~ wherein said DNA vector is a bacterial plasmid.

19. (currently amended) A-The method according to claim 4,
~~characterized in that~~ wherein said DNA vector is a functional plasmid ~~being functional~~ in bacterial cells.

20. (currently amended) A-The method according to claim 4,
~~characterized in that~~ wherein said DNA vector is a functional plasmid ~~being functional~~ in human cells.

21. (currently amended) A-The method according to claim 4,
~~characterized in that~~ wherein the DNA vector is a double strand linear DNA.

22. (currently amended) A-The method according to claim 4,
~~characterized in that~~ wherein the cells transfected in step b)
comprise bacterial cells.

23. (currently amended) A-The method according to claim 4,
~~characterized in that~~ wherein the cells transfected in step b)
consist in-of non human mammalian cells.

24. (currently amended) A-The method according to claim
4, ~~characterized in that~~ wherein the cells transfected in step
b) consist in-of human cells.